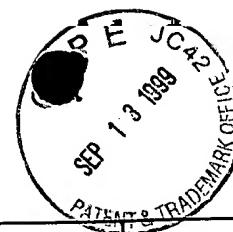


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Sheet 1 of 8

Form 1449*

**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT
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Atty. Docket No.: 103.009US1

Serial No. 09/313,048

Applicant: Dennis A. Carson et al.

Filing Date: May 17, 1999

Group: 1614 1611**U. S. PATENT DOCUMENTS**

**Examiner Initial	Document Number	Date	Name	Class	Subclass	Filing Date If Appropriate
BS	3,127,402	03/31/1964	Pachter et al.	260	251.5	06/23/62 ✓
BS	4,091,219	05/23/1978	Denzel et al.	544	117	09/12/77
BS	4,510,141	04/09/1985	Heckendorf	514	250	09/13/82
BS	4,665,182	05/12/1987	Nichol et al.	544	258	11/19/85
BS	4,701,455	10/20/1987	Nichol et al.	514	249	06/21/85
BS	4,766,133	08/23/1988	Fischli et al.	514	338	08/06/86
BS	4,778,806	10/18/1988	Bender et al.	514	336	08/19/86
BS	4,794,114	12/27/1988	Bender et al.	514	333	06/17/87
BS	4,931,437	06/05/1990	Fedi et al.	514	234.2	08/25/88
BS	5,198,547	03/30/1993	Bailey et al.	544	258	03/16/92
BS	5,288,721	02/22/1994	Klein et al.	514	263	09/22/92
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BS	5,593,992	01/14/1997	Adams et al.	514	235.8	06/07/95
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BS	5,658,903	08/19/1997	Adams et al.	514	253.8	06/03/96
BS	5,670,506	09/23/1997	Leigh et al.	514	258	04/05/93
BS	5,750,575	05/12/1998	Klein et al.	514	617	06/07/95
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**Examiner Initial	Document Number	Date	Country	Class	Subclass	Translation Yes No
BS	0490181	06/17/1992	European	A61K	31/52	
BS	0493682	07/08/1992	European	A61K	31/52	
BS	08-092250	04/09/1996	Japan	C07D	471/04	With Abstract
BS	92/10190	06/22/1992	PCT	A61K	31/44	
BS	92/21344	12/10/1992	PCT	A61K	31/52	
BS	96/40143	12/19/1996	PCT	A61K	31/505	
BS	97/25045	07/17/1997	PCT	A61K	31/505	
BS	97/25047	07/17/1997	PCT	A61K	31/505	
BS	97/25048	07/17/1997	PCT	A61K	31/505	

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(Including Author, Title, Date, Pertinent Pages, Etc.)

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BS	In: <u>Remington's Pharmaceutical Sciences, Eighteenth Edition</u> , Gennaro, A.R., (ed.), Mack Publishing Company, Easton, PA, p. 391 (1990)
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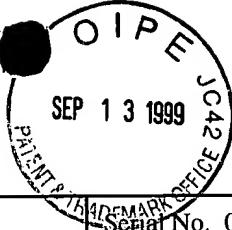
Examiner Ben Shuecole

Date Considered

9/20/99

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Sheet 2 of 8

Form 1449*

Atty. Docket No.: 103.009US1

Serial No. 09/313,048

INFORMATION DISCLOSURE STATEMENT
BY APPLICANT
(Use several sheets if necessary)

Applicant: Dennis A. Carson et al.

Filing Date: May 17, 1999

Group: 1614 1611

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BS	Badger, A.M., et al., "Pharmacological Profile of SB 203580, a Selective Inhibitor of Cytokine Suppressive Binding Protein/p38 Kinase, in Animal Models of Arthritis, Bone Resorption, Endotoxin Shock and Immune Function", <u>The Journal of Pharmacology and Experimental Therapeutics</u> , 279, 1453-1461, (1996) ✓
BS	Baker, J.A., et al., "Synthesis of Derivatives of Thizolo[4,5-d]pyrimidine. Part II", <u>Journal of the Chemical Society (C)</u> , 18, 2478-2484, (1970) ✓
BS	Boehm, J.C., et al., "1-Substituted 4-Aryl-5-pyridinylimidazoles: A New Class of Cytokine Suppressive Drugs with Low 5-Lipoxygenase and Cyclooxygenase Inhibitory Potency", <u>Journal of Medical Chemistry</u> , 39, 3929-3937, (1996) ✓
BS	Boujrad, N., et al., "Inhibition of Hormone-Stimulated Steroidogenesis in Cultured Leydig Tumor Cells by a Cholesterol-Linked Phosphorothioate Oligodeoxynucleotide Antisense to Diazepam-Binding Inhibitor", <u>Proc. Natl. Acad. Sci. USA</u> , 90, 5728-5731, (June 1993) ✓
BS	Burrows, J.L., "Determination of Oxpentifylline and Three Metabolites in Plasma by Automated Capillary Gas Chromatography using Nitrogen-Selective Detection", <u>Journal of Chromatography</u> , 423, 139-146, (1987) ✓
BS	Cembrzynska-Nowak, M., et al., "Elevated Release of Tumor Necrosis Factor-alpha and Interferon-gamma by Bronchoalveolar Leukocytes from Patients with Bronchial Asthma", <u>American Review of Respiratory Diseases</u> , 147, 291-295, (1993) ✓
BS	Chaby, R., "Strategies for the Control of LPS-Mediated Pathophysiological Disorders", <u>Drug Discovery Today</u> , 4, 209-221, (May 1999) ✓
BS	Chaudhri, G., et al., "Reactive Oxygen Species Facilitate in vitro and in vivo Lipopolysaccharide-Induced Release of Tumor Necrosis Factor", <u>The Journal of Immunology</u> , 143, 1290-1294, (Aug. 15, 1989) ✓
BS	Cifone, M.G., et al., "Apoptotic Signaling through CD95 (Fas/Apo-1) Activates an Acidic Sphingomyelinase", <u>The Journal of Experimental Medicine</u> , 177, 1547-1552, (Oct. 1993) ✓
BS	Cottam, H.B., et al., "Substituted Xanthines, Pteridinediones, and Related Compounds as Potential Antiinflammatory Agents. Synthesis and Biological Evaluation of Inhibitors of Tumor Necrosis Factor α ", <u>Journal of Medicinal Chemistry</u> , 39, 2-9, (1996) ✓
BS	Coughlan, A.F., et al., "P-Selectin and Platelet-activating Factor Mediate Initial Endotoxin-induced Neutropenia", <u>The Journal of Experimental Medicine</u> , 179, 329-334, (Jan. 1994) ✓

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Ben Shuele

Date Considered

9/30/99

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Sheet 3 of 8

Form 1449*

Atty. Docket No.: 103.009US1 Serial No. 09/313,048

**INFORMATION DISCLOSURE STATEMENT
BY APPLICANT**
(Use several sheets if necessary)

Applicant: Dennis A. Carson et al.

Filing Date: May 17, 1999

Group: 1614 1611

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BS	Crouch, S.P., et al., "Effect of Ingested Pentoxifylline on Neutrophil Superoxide Anion Production", <u>Infection and Immunity</u> , <u>60</u> , 4504-4509, (Nov. 1992)
BS	Curran, W.V., et al., "Pteridine Chemistry. VII. The Cyanoethylation of Some Hydroxypteridines", <u>Chemical Abstracts</u> , <u>57</u> , As Reported by Smith, M.E., 5920-5922, (1962)
BS	Day, C.P., et al., "Plasma Membrane Form of Phosphatidate Phosphohydrolase: a Possible Role in Signal Transduction During Liver Fibrogenesis", <u>Clinical Science</u> , <u>85</u> , 281-287, (1993)
BS	Dbaibo, G.S., et al., "Tumor Necrosis Factor- α (TNF- α) Signal Transduction through Ceramide", <u>The Journal of Biological Chemistry</u> , <u>268</u> , 17762-17766, (Aug. 25, 1993)
BS	Dinarello, C.A., "Interleukin-1 and Tumor Necrosis Factor: Effector Cytokines in Autoimmune Diseases", <u>Seminars in Immunology</u> , <u>4</u> , 133-145 (1992)
BS	Dressler, K.A., et al., "Tumor Necrosis Factor- α Activates the Sphingomyelin Signal Transduction Pathway in a Cell-Free System", <u>Science</u> , <u>255</u> , 1715-1718, (Mar. 27, 1992)
BS	Gallagher, T.F., et al., "2,4,5-Triarylimidazole Inhibitors of IL-1 Biosynthesis", <u>Bioorganic & Medicinal Chemistry Letters</u> , <u>5</u> , 1171-1176, (1995)
BS	Grabarek, Z., et al., "Zero-Length Crosslinking Procedure with the Use of Active Esters", <u>Analytical Biochemistry</u> , <u>185</u> , 131-135, (1990)
BS	Griswold, D.E., et al., "Differentiation in vivo of Classical Non-Steroidal Antiinflammatory Drugs from Cytokine Suppressive Antiinflammatory Drugs and Other Pharmacological Classes Using Mouse Tumour Necrosis Factor alpha Production", <u>Drugs Under Experimental and Clinical Research</u> , <u>XIX</u> , 243-248, (1993)
BS	Griswold, D.E., et al., "Evaluation of Human Cytokine Production and Effects of Pharmacological Agents in a Heterologous System in Vivo", <u>Journal of Immunological Methods</u> , <u>195</u> , 1-5, (1996)
BS	Haimovitz-Friedman, A., et al., "Ionizing Radiation Acts on Cellular Membranes to Generate Ceramide and Initiate Apoptosis", <u>The Journal of Experimental Medicine</u> , <u>180</u> , 525-535, (Aug. 1994)
BS	Han, H., et al., "5'-Amino Acid Esters of Antiviral Nucleosides, Acyclovir, and AZT Are Absorbed by the Intestinal PEPT1 Peptide Transporter", <u>Pharmaceutical Research</u> , <u>15</u> , 1154-1159, (1998)

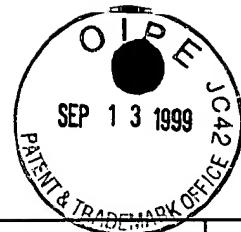
Examiner Ben Shuey

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Sheet 4 of 8

Form 1449*	Atty. Docket No.: 103.009US1	Serial No. 09/313,048
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	Applicant: Dennis A. Carson et al.	
	Filing Date: May 17, 1999	Group: 1614 16 11

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(Including Author, Title, Date, Pertinent Pages, Etc.)

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<i>BS</i>	Hannun, Y.A., et al., "Ceramide: An Intracellular Signal for Apoptosis", <u>TIBS</u> , 20, 73-77, (Feb. 1995)	✓
<i>BS</i>	Hotamisligil, G.S., et al., "Adipose Expression of Tumor Necrosis Factor- α : Direct Role in Obesity-Linked Insulin Resistance", <u>Science</u> , 259, 87-91, (Jan. 1, 1993)	✓
<i>BS</i>	Imagawa, D.K., et al., "The Role of Tumor Necrosis Factor in Allograft Rejection", <u>Transplantation</u> , 51, 57-62, (Jan. 1991)	✓
<i>BS</i>	Jacobs, L.S., et al., "Sphingolipids as Mediators of Effects of Platelet-Derived Growth Factor in Vascular Smooth Muscle Cells", <u>American Journal of Physiology</u> , 265, C740-C747, (Sep. 1993)	✓
<i>BS</i>	Jayadev, S., et al., "Role for Ceramide in Cell Cycle Arrest", <u>The Journal of Biological Chemistry</u> , 270, 2047-2052, (Feb. 3, 1995)	✓
<i>BS</i>	Joseph, C.K., et al., "Bacterial Lipopolysaccharide Has Structural Similarity to Ceramide and Stimulates Ceramide-activated Protein Kinase in Myeloid Cells", <u>The Journal of Biological Chemistry</u> , 269, 17606-17610, (July 1, 1994)	✓
<i>BS</i>	Klein, R.S., et al., "New Synthesis of 5 H-Pyrrolo[3,2-d]pyrimidines via Pyrimido[5,4-c]Pyridazines", <u>Journal of Organic Chemistry</u> , 43, 2536-2539, (1978)	✓
<i>BS</i>	Kumar, S., et al., "Novel Homologues of CSBP/p38 MAP Kinase: Activation, Substrate Specificity and Sensitivity to Inhibition by Pyridinyl Imidazoles", <u>Biochemical and Biophysical Research Communications</u> , 235, 533-538, (1997)	✓
<i>BS</i>	Kurimoto, I., et al., "cis-Urocanic Acid Suppression of Contact Hypersensitivity Induction is Mediated Via Tumor Necrosis Factor- α ", <u>The Journal of Immunology</u> , 148, 3072-3078, (May 15, 1992)	✓
<i>BS</i>	Legrand-Poels, S., et al., "Activation of Human Immunodeficiency Virus Type 1 by Oxidative Stress", <u>AIDS Research and Human Retroviruses</u> , 6, 1389-1397, (1990)	✓
<i>BS</i>	Lister, J.H., et al., In: <u>Fused Pyrimidines -- Part II: Purines</u> , Brown, D.J., (series ed.), John Wiley & Sons, Inc., New York, p. 31-90, (1971)	✓
<i>BS</i>	Lister, J.H., et al., In: <u>Fused Pyrimidines -- Part II: Purines</u> , Brown, D.J., (series ed.), John Wiley & Sons, Inc., New York, p. 220, (1971)	✓
<i>BS</i>	Liu, J., et al., "Renaturation and Tumor Necrosis Factor- α Stimulation of a 97-kDa Ceramide-activated Protein Kinase", <u>The Journal of Biological Chemistry</u> , 269, 3047-3052, (Jan. 28, 1994)	✓

Examiner <i>Ron Schreder</i>	Date Considered <i>9/30/59</i>
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Sheet 5 of 8

Form 1449*

Atty. Docket No.: 103.009US1

Serial No. 09/313,048

**INFORMATION DISCLOSURE STATEMENT
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(Use several sheets if necessary)

Applicant: Dennis A. Carson et al.

Filing Date: May 17, 1999

Group: 1614 1611

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(Including Author, Title, Date, Pertinent Pages, Etc.)

**Examiner
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BS	Liu, M.K., et al., "CD14-Dependent Activation of Protein Kinase C and Mitogen-Activated Protein Kinases (p42 and p44) in Human Monocytes Treated with Bacterial Lipopolysaccharide", <u>The Journal of Immunology</u> , 153, 2642-2652, (1994)	✓
BS	Lømo, J., et al., "TGF-β1 and Cyclic AMP Promote Apoptosis in Resting Human B Lymphocytes", <u>The Journal of Immunology</u> , 154, 1634-1643, (1995)	✓
BS	Lozano, J., et al., "Protein Kinase C ζ Isoform Is Critical for kB-dependent Promoter Activation by Sphingomyelinase", <u>The Journal of Biological Chemistry</u> , 269, 19200-19202, (1994)	✓
BS	Männel, D.N., et al., "Tumor Necrosis Factor: A Cytokine Involved in Toxic Effects of Endotoxin", <u>Reviews of Infectious Diseases</u> , 9, S602-S606, (1987)	✓
BS	Marshall, P.J., et al., "Pharmacology of the Pyrroloimidazole, SK&F 105809-I", <u>Biochemical Pharmacology</u> , 42, 813-824, (1991)	✓
BS	Mathias, S., et al., "Activation of the Sphingomyelin Signaling Pathway in Intact EL4 Cells and in a Cell-Free System by IL-1 β", <u>Science</u> , 259, 519-522, (Jan. 22, 1993)	✓
BS	Matsuyama, T., et al., "Cytokines and HIV Infection: is AIDS a Tumor Necrosis Factor Disease?", <u>AIDS</u> , 5, 1405-1417, (1991)	✓
BS	Meskini, N., et al., "Phosphodiesterase Inhibitory Profile of Some Related Xanthine Derivatives Pharmacologically Active on the Peripheral Microcirculation", <u>Biochemical Pharmacology</u> , 47, 781-788, (1994)	✓
BS	Moreira, R., et al., "A New Direct Synthesis of Tertiary N-Acyloxymethylamide Prodrugs of Carboxylic Acid Drugs", <u>Tetrahedron Letters</u> , 35, 7107-7110, (1994)	✓
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BS	Opal, S.M., et al., "Clinical Trials for Severe Sepsis", <u>Infectious Disease Clinics of North America</u> , 13, 285-297, (June 1999)	✓
BS	Peterson, T.C., "Pentoxifylline Prevents Fibrosis in an Animal Model and Inhibits Platelet-derived Growth Factor-driven Proliferation of Fibroblasts", <u>Hepatology</u> , 17, 486-493, (1993)	✓

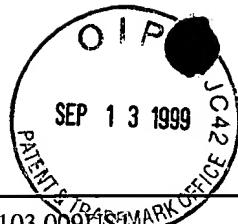
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Sheet 6 of 8

Form 1449*

Atty. Docket No.: 103.009 GS

Serial No. 09/313,048

INFORMATION DISCLOSURE STATEMENT
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Applicant: Dennis A. Carson et al.

Filing Date: May 17, 1999

Group: 1614 / 6 / 11

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(Including Author, Title, Date, Pertinent Pages, Etc.)

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BS	Raines, M.A., et al., "Sphingomyelinase and Ceramide Activate Mitogen-Activated Protein Kinase in Myeloid HL-60 Cells", <u>The Journal of Biological Chemistry</u> , 268, 14572-14575, (July 15, 1993)
BS	Rice, G.C., et al., "Protection from Endotoxic Shock in Mice by Pharmacologic Inhibition of Phosphatidic Acid", <u>Proc. Natl. Acad. Sci. USA</u> , 91, 3857-3861, (Apr. 1994)
BS	Ridley, S.H., et al., "Actions of IL-1 are Selectively Controlled by p38 Mitogen-Activated Protein Kinase", <u>The Journal of Immunology</u> , 158, 3165-3173, (1997)
BS	Rivas, C.I., et al., "Involvement of the Sphingomyelin Pathway in Autocrine Tumor Necrosis Factor Signaling for Human Immunodeficiency Virus Production in Chronically Infected HL-60 Cells", <u>Blood</u> , 83, 2191-2197, (Apr. 15, 1994)
BS	Schrage, A., et al., "Studies on Condensed Pyrimidine Systems. V. (1) The Pyrimido[4,5-c][1,2,5]thiadiazole Ring System", <u>Journal of Organic Chemistry</u> , 16, 207-215, (1951)
BS	Seekamp, A., et al., "Ischemia - Reperfusion Injury", <u>Agents and Actions Supplements</u> , 41, 137-152, (1993)
BS	Semmler, J., et al., "Xanthine Derivatives: Comparison between Suppression of Tumour Necrosis Factor- α Production and Inhibition of cAMP Phosphodiesterase Activity", <u>Immunology</u> , 78, 520-525, (1993)
BS	Sharief, M.K., et al., "Elevated Serum Levels of Tumor Necrosis Factor- α in Guillain-Barré Syndrome", <u>Annals of Neurology</u> , 33, 591-596, (June 1993)
BS	Sliwa, K., et al., "Randomised Investigation of Effects of Pentoxyfylline on Left-Ventricular Performance in Idiopathic Dilated Cardiomyopathy", <u>The Lancet</u> , 351, 1091-1093, (Apr. 11, 1998)
BS	Staros, J.V., et al., "Enhancement by N-Hydroxysulfosuccinimide of Water-Soluble Carbodiimide-Mediated Coupling Reactions", <u>Analytical Biochemistry</u> , 156, 220-222, (1986)
BS	Strieter, R.M., et al., "Cellular and Molecular Regulation of Tumor Necrosis Factor-alpha Production by Pentoxyfylline", <u>Biochemical and Biophysical Research Communications</u> , 155, 1230-1236, (Sep. 30, 1988)
BS	Timmis, G.M., "A New Synthesis of Pteridines", <u>Nature</u> , 164, 139, (July 23, 1949)
BS	Tracey, K.J., et al., "Cachectin/Tumor Necrosis Factor Induces Cachexia, Anemia, and Inflammation", <u>Journal of Experimental Medicine</u> , 167, 1211-1227, (Mar. 1988)

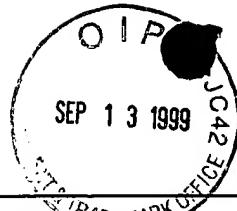
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Sheet 7 of 8

Form 1449*	Atty. Docket No.: 103.009US	Serial No. 09/313,048
INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use several sheets if necessary)	Applicant: Dennis A. Carson et al.	
	Filing Date: May 17, 1999	Group: 1614 1611

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(Including Author, Title, Date, Pertinent Pages, Etc.)

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<i>BS</i>	Venable, M.E., et al., "Identification of a Defect in the Phospholipase D/Diacylglycerol Pathway in Cellular Senescence", <u>The Journal of Biological Chemistry</u> , 269, 26040-26044, (Oct. 21, 1994)
<i>BS</i>	Verheij, M., et al., "Requirement for Ceramide-Initiated SAPK/JNK Signalling in Stress-Induced Apoptosis", <u>Nature</u> , 380, 75-79, (Mar. 7, 1996) ✓
<i>BS</i>	Ward, A., et al., "Pentoxifylline -- A Review of its Pharmacodynamic and Pharmacokinetic Properties, and its Therapeutic Efficacy", <u>Drugs</u> , 34, 50-97, (1987) ✓
<i>BS</i>	Wilson, K.P., et al., "The Structural Basis for the Specificity of Pyridinylimidazole Inhibitors of p38 MAP Kinase", <u>Chemistry & Biology</u> , 4, 423-431, (June 1997) ✓
<i>BS</i>	Wolff, R.A., et al., "Role of Ceramide-activated Protein Phosphatase in Ceramide-mediated Signal Transduction", <u>The Journal of Biological Chemistry</u> , 269, 19605-19609, (July 29, 1994) ✓
<i>BS</i>	Wu, J., et al., "Inhibition of the EGF-Activated MAP Kinase Signaling Pathway by Adenosine 3',5' Monophosphate", <u>Science</u> , 262, 1065-1069, (Nov. 12, 1993) ✓
<i>BS</i>	Yanagawa, H., et al., "Analysis of Superhelical Structures of Nucleic Acid-Lipid Conjugates by Image Processing", <u>Nucleic Acids Research, Symposium Series No. 19</u> , Symposium on Nucleic Acids Technology, Okayama, Japan, 189-192, (Feb. 20-21, 1988) ✓

Examiner <i>Ben Schreder</i>	Date Considered <i>9/30/99</i>
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